REMARKS

Claims 44 and 47 presently appear in this case. Claim 44 has been withdrawn from consideration. No claims have been allowed. The Official Action of June 14, 2011, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a pH-independent extended release dosage form of venlafaxine hydrochloride. The venlafaxine hydrochloride is coated on a nonpareil core over which is coated a controlled release layer, which is a ethyl cellulose mixed with a dibutyl cebacate plasticizer. The controlled release layer permits controlled release of the venlafaxine hydrochloride over an approximately 24 hour period. An intermediate isolating layer of polyvinylpyrrolidone is also present. The pH-independent extended release dosage form has dissolution characteristics that are equivalent to those of the venlafaxine hydrochloride dosage forms sold under the proprietary name EFFEXOR XR.

Interview between Examiner Vu and the undersigned attorney conducted on September 14, 2011, is hereby gratefully acknowledged. At the outset, the examiner was shown the proposed amendments to the claims presented herein. It was

pointed out that claim 47 had been amended to insert the subject matter of claim 48 and the identity of the plasticizer. Other than non-elected claim 44, which was amended to depend from claim 47, all of the other claims were deleted. The examiner said that the amendment certainly eliminated the 112 rejection and would likely overcome the obviousness rejections, although the examiner stated that he would need to give it a final review and bring his search up to date before concluding that the remaining claims were allowable.

In the Office Action of June 14, 2011, the examiner states that claim 44 has been withdrawn from consideration because it lacks unity with the invention originally claimed. Claim 44 has now been amended to depend from claim 47. If claim 47 is deemed to be allowable then method of use claim 44 should be rejoined, examined and allowed with claim 47.

Claim 47 has been rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement. The examiner states that the claim is rejected because it does not identify the structure, material or acts set forth in the specification that would be capable of carrying out the functional properties recited in the claims, such as

"equivalent to the dissolution characteristics to EFFEXOR XR." This rejection is respectfully traversed.

Claim 48 was not made subject to this rejection. The subject matter of claim 48 has now been added to claim 47. Accordingly, claim 47 is effectively now claim 48 rewritten into independent form. The specific materials that that are capable of carrying out the functional properties are now recited in the claim. Accordingly, this rejection is now moot. Reconsideration and withdrawal thereof is respectfully urged.

Claims 29-40, 42, 43, and 46-49 have been rejected under 35 USC 103(a) as being unpatentable over Heiligenstein. The examiner states that Heiligenstein's composition is inherently capable of meeting the limitation of release of the venlafaxine hydrochloride over an approximately 24 hour period after oral administration as the same ingredients are used, such as, hydroxypropyl methylcellulose. This rejection is respectfully traversed.

The claims have now been amended to include only the specific composition that is known to be bioequivalent to EFFEXOR XR. These ingredients do not include hydroxypropyl methylcellulose. Accordingly, the present claims do no read on the composition of Heiligenstein as the ingredients now claimed

permit 24 hour sustained release and Heiligenstein's compositions are incapable of such properties. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 29-40, 42, 43 and 46-49 have been rejected under 35 USC 103(a) as being unpatentable over Oshlack in view of Sherman and Palomo Coll, as evidenced by an FDA Guidance for Industry (2002), hereinafter "FDA." The examiner states that Oshlack teaches an extended release drug composition with all of applicant's claimed layers but not teaching use of venlafaxine hydrochloride as the drug or the use of a separation layer such as polyvinylpyrrolidone. The examiner states that Sherman teaches a composition for extended release of venlafaxine hydrochloride using a film coating of ethyl cellulose to retard dissolution for extended release. The examiner states that Palomo Coll teaches that separation layers made from hydroxypropylmethylcellulose and polyvinylpyrrolidone are well known in the art. The examiner considers that it would have been obvious to incorporate venlafaxine into Oshlack's composition in order to improve the stability of the venlafaxine composition and still have 24 hour extended release of the drug. The examiner considers that it would have been obvious to

incorporate a separation layer into Oshlack's composition as polyvinylpyrrolidone and hydroxypropylmethylcellulose are functional equivalents used as separation layers in drug formulation. The examiner considers that optimization of parameters is a routine practice that would have been obvious in order to achieve, for example, a drug release rate to meet the requirement of the FDA publication for a generic drug to be bioequivalent by dissolution studies to the reference drug. This rejection is respectfully traversed.

Claim 47 now claims a very particular composition, with particular amounts, in order to achieve specific dissolution properties which are bioequivalent to EFFEXOR XR. This particular claimed composition would not have been obvious from the combination of references. In this regard, the examiner's attention is invited to the recent Federal Circuit decision in *Unigene v Apotex*, No. 2010-1006, 2011 U.S. App. LEXIS 17762, Fed. Cir 2011. A copy of this decision was left with the examiner at the interview. This case was directed to a determination of the obviousness of the claims of a patent directed to a composition that was bioequivalent to a specific FDA-approved pharmaceutical. In *Unigene*, as in this case, there was a design need to achieve a bioequivalent composition and a

market demand to achieve a composition that treats the same symptoms as the reference formulation (see slip opinion page 22).

Unigene explains the law of obvious to try at slip opinion page 20-21, where it states:

> To render a claim obvious, prior art cannot be "vague" and must collectively, although not explicitly, guide an artisan of ordinary skill towards a particular solution. *Bayer Schering*, 575 F.3d at 1347. Indeed, "most inventions that are obvious were also obvious to try," *id.*, and a combination is only obvious to try if a person of ordinary skill has "a good reason to pursue the known options." *KSR*, 550 U.S. at 421. When a field is "unreduced by direction of the prior art," and when prior art gives "no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful," an invention is not obvious to try. *Bayer Schering*, 575 F.3d at 1347 (citing *O'Farrell*, 853 F.2d at 903); *see also Ortho-McNeil*, 520 F.3d at 1364 (stating the number of options must be "small or easily traversed").

Unigene teaches that in cases such as this, the reference composition is that of the FDA-approved composition to which the present composition is intended to be bioequivalent, in this case the composition of Sherman. The secondary publications must make obvious each of the changes made to Sherman in order to come up with a bioequivalent formulation. Here, the claimed

composition would not have been obvious to try from the compositions of the prior art as the prior art gives no indication of whch parameters were critical and no direction as to which of many possible choices is likely to be successful. The same is true of the claimed amounts. The examiner states, without support, that the specific amounts are result effective parameters that a person of ordinary skill in the art would routinely optimize. However, here, the result is bioequivalence to EFFEXOR XR. There is no direction in the art as to what components and amounts are to be tried or how varying the amounts or the compounds would be expected to affect bioequivalence.

As stated in the penultimate paragraph of *Unigene*, and as is true *mutatis mutandis* for the present case:

> Thus, even accepting that there was a design need and market pressure to develop a pharmaceutical formulation that is bioequivalent to Miacalcin®, there is no evidence in the record that claim 19 would be an obvious solution to those motivations.

For all of these reasons reconsideration and withdrawal of this rejection for the single composition claim now directed only to the specific composition found to be bioequivalent to EFFEXOR XR, are earnestly solicited.

It is submitted that all of the claims now present in the case clearly define over the references of record and fully comply with 35 USC §112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant

By: /rlb/
Roger L. Browdy
Registration No. 25,618

RLB:jhw
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528